

USDA Dietary Supplement Ingredient Database Release 2.0

DSID-2

Background Information and Pilot Study Research Summary

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1. Introduction

The Nutrient Data Laboratory (NDL), Beltsville Human Nutrition Research Center (BHNRC), Agricultural Research Service (ARS), USDA, has been working with the Office of Dietary Supplements, National Institutes of Health (ODS/NIH) and other federal agencies to develop a Dietary Supplement Ingredient Database (DSID) to evaluate levels of ingredients in dietary supplement products. The DSID is funded, in large part, by the Office of Dietary Supplements. It builds on the well-recognized strengths of the USDA/ARS in developing databases that support the assessment of intake of nutrients from foods (<http://www.ars.usda.gov/nutrientdata>). ODS provides leadership, jointly with its federal partners, in making this a reality. The consortium of federal agencies includes ODS and partners at USDA/ARS, the National Center for Health Statistics of the Centers for Disease Control and Prevention (NCHS/CDC), The Food and Drug Administration (FDA), the National Cancer Institute (NCI), NIH, and the National Institute of Standards and Technology (NIST) of the Department of Commerce.

The goals for the Dietary Supplement Ingredient Database (DSID) are to:

- Develop reliable baseline estimates of ingredients and other bioactive components in dietary supplement products.
- Report on analyzed levels of ingredients relative to labeled values.
- Support improved dietary intake assessments in research by providing analytical estimates of the ingredient content of marketed dietary supplements.
- Release and maintain a publicly available on-line composition database for dietary supplements.

This database will give researchers and healthcare professionals access to information on analytically validated levels of ingredients in a variety of dietary supplements including multivitamin/mineral products (MVMs¹), single ingredient products, fish oil products containing omega-3-fatty acids, and botanically-based supplements.

The Dietary Supplement Health and Education Act (DSHEA) of 1994, defines a dietary supplement as:

- A product (other than tobacco) that is intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients.
- Intended for ingestion in pill, capsule, tablet, or liquid form.
- Not represented for use as a conventional food or as the sole item of a meal or diet.
- Labeled as a "dietary supplement."

¹There are many definitions for the terms multivitamin and multivitamin/multimineral (MVM). For the DSID studies, the definition of MVM is based on the NCHS/CDC paper in which multivitamin/mineral products are defined as containing "three or more vitamins with or without minerals" (Radimer et al., 2004).

2. Background

In 2004, the consortium of federal agencies listed above identified DSID priorities for products and ingredients of public health and research interest. The initial prioritization of product types was determined by evaluating reported consumption patterns of dietary supplements from the NHANES 1999-2000 dietary supplement data file. (NHANES provides information obtained from nearly 5,000 individuals annually, including food intake records assessed with two 24-hour dietary recalls plus reported dietary supplement intake over the previous month). Adult multivitamin/mineral (MVM) products were identified as a top priority because they are the most commonly reported dietary supplement in NHANES surveys. Other highly ranked supplement product categories initially identified for chemical analysis due to high weighted frequency of use were children's and prenatal MVMs, calcium supplements and vitamin E, vitamin C, and B-vitamin products.

In order to set priorities for ingredient analysis, dietary supplement ingredients were ranked using a weighting system that included the following factors: population exposure based upon frequency of reported use, NIH research interest, availability of valid analytical methods and measurement capabilities, and public health importance (Dwyer et. al., 2006). Each factor was assigned a weight based on the relative importance and each item was scored for that factor. The sums of the weighted scores were then rank ordered to yield a priority list. Ingredients of lower priority will be considered for study in later phases of DSID research (Dwyer et al., 2007). Pilot studies were conducted to address key challenges of dietary supplement laboratory analysis, including evaluation of sample handling procedures and analytical methods

3. Pilot Studies

A. Laboratory and Analytical Methods Pilot Study

In order to qualify laboratories for the analysis of ingredients in supplement products, sample preparation and method protocols for priority vitamins and minerals in adult MVM products were assessed and evaluated. The priority ingredients evaluated included: folic acid, vitamin C, vitamin A (retinol and beta-carotene), vitamin E (alpha-tocopherol), calcium, iron, riboflavin, thiamin, niacin, vitamin B-6, vitamin B-12, vitamin D, phosphorus, potassium, copper, selenium, chromium, manganese, magnesium, zinc, and iodine.

Four commercial or academic laboratories analyzed each priority nutrient in two MVM products five times over a period of several months. One of these MVM products was National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 3280, under development at the time of the study. The mean and variability for each nutrient in each lab were reviewed, compared to the preliminary NIST results and presented to a federal working group. For each new study for the DSID, these initial

assessments of acceptable laboratory and method variability continue to be re-evaluated.

Pilot study findings:

The expert federal working group identified acceptable method variability and acceptable labs for future DSID analytical work. More details on this study have been published (Roseland et al., 2008). A copy of the journal article is available at: http://www.ars.usda.gov/SP2UserFiles/Place/12354500/Articles/JFCA21_S69-S77.pdf

B. Adult MVM Common Level Pilot Study

The adult MVM common level (CL) pilot study was designed and conducted with the following objectives:

- To determine if systematic relationships exist between label and analytical values for nutrients in adult multivitamin/mineral (MVM) products
- To assess the nutrient variability between products labeled at up to four of the most common labeled levels for each priority vitamin and mineral
- To evaluate this common level (CL) approach for planning future studies

In order to identify the most common labeled levels for priority vitamins and minerals in adult MVMs, the NHANES 2001-02 data file was evaluated. The nutrients evaluated were vitamins C, E, B-6, B-12, folic acid, niacin, riboflavin, thiamin, calcium, iron, copper, iodine, magnesium, manganese, phosphorus, potassium, selenium, and zinc. Using the previously described MVM definition, 541 supplements were identified as adult MVM products. The weighted frequency of each product was calculated and applied to its labeled ingredients. The total weighted frequency for each labeled level within each ingredient was then calculated and distribution graphs evaluated. In most cases, there were three or four most common labeled levels per ingredient. The most common labeled level for many of the vitamins and minerals was 100% of the Daily Value.

Representative adult MVM products with ingredients at these levels were identified for analysis with a sampling plan with probability proportional to size (in this case, weighted frequency). A total of 219 different MVM products were purchased locally, including six products from each CL for each ingredient.

After purchase, products were repackaged and sent to analytical laboratories in defined batches for the analysis of eight vitamins and ten minerals. Quality control (QC) materials, including standard reference materials (SRMs), blinded duplicates and in-house control materials were added to each batch of samples in order to evaluate laboratory precision and accuracy on an on-going basis. Qualified analytical contract and cooperating laboratories analyzed the sample sets using validated sample-handling protocols and appropriate methods, to obtain analytical data about the levels of these

nutrients in adult MVM supplements. Most of the vitamins were analyzed by validated high performance liquid chromatography (HPLC) methods, while most of the minerals were analyzed by inductively coupled plasma spectrometry (ICP) techniques. Six products at each CL were analyzed; over 500 nutrient analyses were completed.

Pilot study findings:

Analysis of pilot study results focused on comparing analytical results to labeled nutrient levels for each nutrient. Laboratory results were statistically evaluated for each nutrient (typically n=18 or 24) at each common level (n=6 products).

For 12 nutrients analyzed in this study (magnesium, iron, niacin, zinc, phosphorus, potassium, calcium, manganese, thiamin, vitamin B-6, vitamin C, and riboflavin), the mean % differences from label and standard deviation were both less than 10%, indicating that the analytical results for these nutrients in MVM products were consistently close to labeled levels across the common levels evaluated. One ingredient, selenium, had a mean % difference from label that was >20% above label and significantly different from label for all the levels analyzed. Results were more variable for the five other vitamins and minerals studied (vitamin E, copper, vitamin B-12, folic acid and iodine). The findings from this study facilitated development of a comprehensive analytical study of adult MVMs.

C. Caffeine Pilot Study

In order to gather some preliminary information on the prevalence of caffeine in selected dietary supplements, the NDL planned a pilot study to identify representative dietary supplement products containing caffeine and to determine the analytical caffeine content (Andrews et al., 2007). This study was intended to be a snapshot look at the products currently being sold in the U.S. The products identified for analysis were predominantly sports performance and weight loss supplements, which represent the segment of the dietary supplement market that is most likely to contain caffeine. Caffeine-containing dietary supplements were selected when labels listed one or more of the following ingredients: caffeine, guarana, yerba mate, cocoa, kola, green tea and citrus aurantium.

Products were selected based on the estimated market share for three categories determined from Nutrition Business Journal and AC Nielsen data (2004):

- Health food/natural foods (30.1%)
- Mass merchandisers, including supermarkets and drug stores (25.4%)
- Direct channels, including multi-level marketers, internet, catalog and practitioners (44.5%)

Approximately 50 dietary supplements sold in these channels were purchased and analyzed for their caffeine content. Two to three lots of each product were purchased over a period of nine months.

An independent laboratory experienced with caffeine analysis and botanical matrices analyzed the dietary supplements for their caffeine content. Rigorous QC measures, including the analysis of standard reference materials (SRMs), were implemented. Two SRMs were analyzed with each batch of supplements. One SRM, NIST SRM 3243 Ephedra-Containing Solid Oral Dosage Form, was a diet pill mixture with a certified level of 76.5 mg/g caffeine. The other SRM, NIST SRM 3244 Ephedra-Containing Protein Powder, was a cocoa-protein powder with a certified level of 2.99 mg/g caffeine. Analytical caffeine values for both reference materials were within the certified range of the materials, indicating acceptable accuracy and precision for the product results.

Pilot study findings:

Results have been calculated in mg caffeine/day, because label instructions varied so widely among the products (from 1 tablet/day to 4 tablets/serving and 3 servings/day). Laboratory analysis for all 53 products showed product means ranging from 0.07 to 307 mg caffeine/tablet and 1 to 829 mg caffeine/day. According to the USDA food composition database (U.S. Dept. of Agriculture, 2011), one cup of brewed coffee contains approximately 95 mg/caffeine. Using this value as a reference, the 53 products analyzed provide a range of caffeine levels that correspond to the caffeine levels in 0 - 8 cups of brewed coffee/day.

Caffeine intakes from the dietary supplement products analyzed in this study ranged from 1 mg to greater than 800 mg/day, if taken at maximum recommended dosages. For most (89%) of the caffeine-containing dietary supplements that listed a level of caffeine on the label, the mean analyzed level calculated on a per day basis was similar to the labeled amount (within 20%). Most products (72%) showed a lot-to-lot variability of less than 10%.

In the U.S., dietary supplement products may contain caffeine in proprietary blends or from botanical sources (e.g. guarana, yerba mate, cocoa, kola nut and green tea extract) even if caffeine is not listed as an ingredient on the label.

4. Nationwide DSID Studies

After the completion of these pilot studies, two national studies of ingredients in MVMs were completed. A study of adult MVMs was conducted to estimate national estimates for the relationship between label values and analytical values for 18 vitamins and minerals. For more information about this study, please read the Adult MVM Research Summary, available on the DSID-2 website. The statistical results for this study and NHANES application tables have also been released in DSID-2 (<http://dsid.usda.nih.gov>).

Adult MVM results were originally released in DSID-1 in April, 2009. DSID-1 adult MVM results have been replaced with updated data for selected ingredients and statistical

updates for additional ingredients. For more information, see section 6A of the Adult MVM Research Summary, Adjustments to Data for DSID-2.

A study of children's MVMs was conducted to establish national estimates for the relationship between label values and analytical values for priority vitamins and minerals. For more information about this study, please read the Children's MVM Research Summary, available on the DSID-2 website. The statistical results for this study and NHANES application tables have also been released in DSID-2 (<http://dsid.usda.nih.gov>).

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